B1 20. (Once Amended) A monoclonal antibody or antigen binding fragment according to Claim 19, secreted by the hybridoma cell line deposited at CNCM under Accession No. I-1397.

B2 24. (Once Amended) A method for the treatment of cancer in an individual comprising administering to said individual [an] a therapeutically effective amount of a monoclonal antibody according to Claim 19 so as to [affect the immune system of] elicit an anti-tumor effect in the treated individual.

B3 26. (Once Amended) A pharmaceutical composition comprising, as an active ingredient, [an] a therapeutically effective amount of a monoclonal antibody according to Claim 19 so as to elicit an anti-tumor effect in the treated individual, and a physiologically acceptable carrier.

REMARKS

Claims 19, 20, 24 and 26 have been amended to describe the claimed subject matter more clearly. The amendments do not introduce new matter within the meaning of 35 U.S.C. § 132. Accordingly, entry of the amendments is respectfully requested.

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Objection to Drawings

The drawings have been objected to because the subfigures of Figures 1-4 are not separately labeled.

Formal drawings separately labeling the subfigures of Figures 1-4 will be submitted upon indication of allowable subject matter by the Examiner.

Accordingly, applicants respectfully request the Examiner to reconsider and withdraw this objection.

Objection to Disclosure

The disclosure has been objected to because of informalities. As the basis of this objection, the Examiner contends:

> The subfigures of Figure 4 are labeled 4(1)-4(4), while subfigures for Figures 1-3 are labeled with Arabic letters. Subfigures 1A-1F, 2A-2B, 3A-3B and those in Figure 4 are not separately described in the Brief Description of Drawings.

In the specification, the Brief Description of the Drawings has been amended to replace subfigures 1-4 of Figure 4 with A-D. Additionally, applicants propose that Figure 4 be similarly amended (see attached Figure 4 with proposed amendments shown in red). The proposed amendments are believed to obviate the objection to the subfigures of Figure 4.

Applicants respectfully traverse the objection to subfigures 1A-1F, 2A-2B, 3A-3B and those in Figure 4 as not being separately

described in the Brief Description of the Drawings. A description of each subfigure appears in The Brief Description of the Drawings on pages 9-11. It is clear to one of ordinary skill in the art that the descriptions of the subfigures are modifications of the general descriptions of Figures 1, 2 and 3. For example, subfigures 1B-F show flow cytometry analysis readings of different monoclonal antibodies while subfigure 1A shows the background reading without a BAT antibody.

Based on the foregoing, applicants respectfully request the Examiner to reconsider and withdraw this objection.

Rejection of Claims 19-27 under 35 U.S.C. § 112, ¶ 1

Claims 19-27 have been rejected under 35 U.S.C. § 112, first paragraph, because the specification lacks complete deposit information for the hybridoma cell line CNCM Accession No. I-1397.

Applicants submit herewith a copy of the Declaration of Dr. Pnina Fischman and a copy of the official receipt from the CNCM depository as filed with applicants' response of August 28, 1996, along with a copy of the stamped filing receipt verifying their original date of filing.

Based on the foregoing, applicants respectfully request the Examiner to reconsider and withdraw this rejection.

Objection to the Specification under 35 U.S.C. § 112, ¶ 1

The specification has been objected to under 35 U.S.C. § 112, first paragraph, as failing to provide an enabling disclosure commensurate with the scope of the claims.

As the basis of this objection, the Examiner contends:

a. In part ii, claim 19 is broadly drawn to "a monoclonal antibody which binds to an antigen which the antibody under (i) binds." Thus, the claim is drawn to any antibody that binds to the protein recognized by the monoclonal antibody of I-1397, not antibodies that recognize the same antigenic epitope as I-1397. The specification discloses only that the antibody produced by I-1397 binds "to a proteinaceous substance having an apparent molecular weight of 48-50K Daltons, as determined by SDS-PAGE" (see p. 7, lines 23-24). With only this information, it would require undue experimentation for one of skill in the art to identify the antibodies claimed.

b. Claims 24-25 are drawn to the treatment of tumors and cancer, and can be broadly interpreted to read on the treatment of any human tumor or cancer with the monoclonal antibodies of the invention. Claims 26-27 are drawn to a pharmaceutical composition, are also broadly interpreted to read on the treatment of human tumors with monoclonal antibodies. Thus, the present invention pertains to the experimental and unpredictable area of the in vivo treatment of human tumors by the administration of immunoglobins. As set forth in paragraph 8e of the previous office action, the difficulties associated with the development of effective antibody-based therapies for human cancers are well established in the art. To further illustrate the state of the art, Hird and Epenetos (Immunotherapy with Monoclonal Antibodies, 1990), which states that "data obtained from mouse studies are useful, but cannot be directly translated to apply to the human situation" (p. 185) is also cited.

Applicants respectfully traverse this objection.

In response to part (a) of this objection, claim 19 has been amended to recite a monoclonal antibody which recognizes the same antigenic epitope as the monoclonal antibody secreted by the I-1397 hybridoma cell line.

In response to part (b) of this objection, applicants submit herewith a Declaration of inventor Dr. Britta Hardy. The Declaration presents experimental results showing the anti-tumor activity of the monoclonal antibody of the invention in mice bearing human tumors. The results also show that the monoclonal antibody of the invention is capable of inducing human tumor regression mediated by stimulation of human immunocytes. These results strongly support the ability of the claimed methods to effectively treat human tumors.

Based on the foregoing, applicants respectfully request the Examiner to reconsider and withdraw this objection.

Rejection of Claims 19-27 under 35 U.S.C. § 112, ¶ 1

Claims 19-27 have been rejected under 35 U.S.C. § 112, first paragraph, for the reasons set forth in the objection to the specification.

Applicants respectfully traverse this rejection for the reasons identified above in the response to the objection to the specification, herein incorporated by reference to avoid

repetition.

Accordingly, applicants respectfully request the Examiner to reconsider and withdraw this rejection.

Rejection of Claims 20 and 24-27 under 35 U.S.C. § 112, ¶ 2

Claims 20 and 24-27 have been rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention.

As the basis of this rejection, the Examiner contends:

> a. The recitation "A monoclonal antibody... according to claim 19" lacks clear antecedent basis in claim 19, as there are three different recitations of monoclonal antibody in claim 19.
> b. The metes and bounds of "fragment" in claim 20 are unclear. It is unclear what type of fragments are encompassed by the claim. The applicant is advised to amend the claim to recite "antigen binding fragment."
> c. The recitation "an effective amount" in claims 24 and 26 is vague and indefinite, as it is unclear what effect is to be achieved by the claimed method and composition.
> d. Claim 24 is vague and indefinite in the recitation "so as to affect the immune system." As the specific effect to be accomplished by the claimed method is unclear, the metes and bounds of the claims are unclear.

To overcome this rejection, applicants have amended the claims as follows:

(1) deleted the second and third recitations of "a monoclonal antibody" in claim 19;

(2) amended claim 20 to recite "antigen binding fragment"; and

(3) amended claims 24 and 26 to recite "a therapeutically effective amount of a monoclonal antibody according to claim 19 so as to elicit an anti-tumor effect in the treated individual". The basis for this amendment is found on page 4, lines 18-22 of the specification. Additionally, the specification defines "anti-tumor effect" on page 4, lines 23-28, and "effective amount" on page 6, lines 6-14.

The foregoing amendments to claims 19, 20, 24 and 26 are believed to obviate this rejection.

Accordingly, applicants respectfully request the Examiner to reconsider and withdraw this rejection.

Rejection of Claims 19, 21-22, 24 and 26 under 35 U.S.C. § 102(b)

Claims 19, 21-22, 24 and 26 have been rejected under 35 U.S.C. § 102(b) as anticipated by Ledbetter (U.S. Patent No. 5,182,368).

As the basis of this rejection, the Examiner contends:

> In part ii, the antibody of claim 19 is broadly drawn to "a monoclonal antibody which binds to an antigen which the antibody under (i) binds." Thus, the claim is drawn to any antibody that binds to the protein recognized by the monoclonal antibody of I-1397, not just antibodies that recognize the same antigenic epitope as I-1397. The specification discloses that the antibody produced by I-1397 binds "to a proteinaceous substance having an

apparent molecular weight of 48-50K Daltons, as determined by molecular weight" (see p. 7, lines 23-24). Ledbetter discloses a monoclonal antibody that recognizes a polypeptide of approximately 50 Kd (see p. 18, lines 45-56), the hybridoma cell line that produces said monoclonal and the use of this antibody to effect the immune system (column 20, lines 1-10). While the antibody of Ledbetter binds to an epitope present only on B cells, there is no evidence of record that the antibody of Ledbetter and I-1397 recognize distinct protein antigens.

The foregoing amendment to claim 19 obviates this rejection.

Ledbetter teaches an antibody that recognizes a polypeptide of approximately 50 Kd and binds only to an epitope present in B cells. By contrast, the claims as presently amended recite a monoclonal antibody that is secreted by the hybridoma cell line deposited at the Collection Nationale de Cultures de Microorganismes (CNCM), under Accession No. I-1397, or recognizes the same antigenic epitope as a monoclonal antibody that is secreted by the I-1397 hybridoma cell line.

To constitute anticipation under 35 U.S.C. § 102, all material elements of a claim must be formed in one prior art source. In re Marshall, 577 F.2d 301, 198 USPQ 344 (CCPA 1978); In re Kalm, 378 F.2d 959, 154 USPQ 10 (CCPA 1967). The Ledbetter patent does not anticipate applicants' claims because it fails to teach a monoclonal antibody that is secreted by the hybridoma cell line deposited at the Collection Nationale de Cultures de Microorganismes (CNCM), under Accession No. I-1397, or a monoclonal

antibody that recognizes the same antigenic epitope as a monoclonal antibody is secreted by the I-1397 hybridoma cell line.

Based on the foregoing, applicants respectfully request the Examiner to reconsider and withdraw this rejection.

CONCLUSION

Based upon the above amendments and remarks, the presently claimed subject matter is believed to be novel and patentably distinguishable over the prior art of record. Accordingly, the Examiner is respectfully requested to reconsider and withdraw the rejections of claims 1-16 and allow all pending claims presented herein for reconsideration.

The Examiner is welcomed to telephone the undersigned attorney if she has any questions or comments.

Respectfully submitted,

NATH & ASSOCIATES

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